

# POLYCYSTIC OVARIAN DISEASE & ENDOMETRIOSIS

{ ومن لم يذق مرّ التعلّم ساعةً.. تجرع ذلّ الجهل طوال حياته }



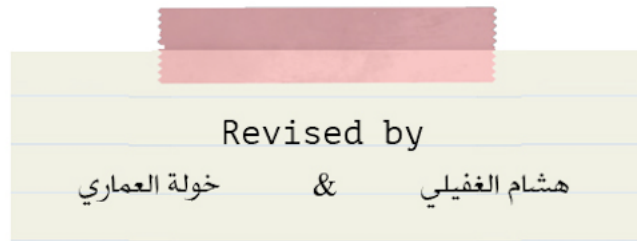
## Lecture Six

### Objectives:

At the end of this lecture, the student should be able to:

- Know the clinicopathologic features of endometriosis with special emphasis on: definition, typical sites and theories behind its pathogenesis.
- Understand the clinical manifestations and pathologic features of polycystic ovarian disease.

References: Lecture slides & Robbins



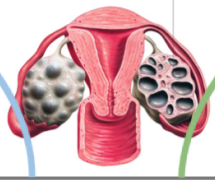
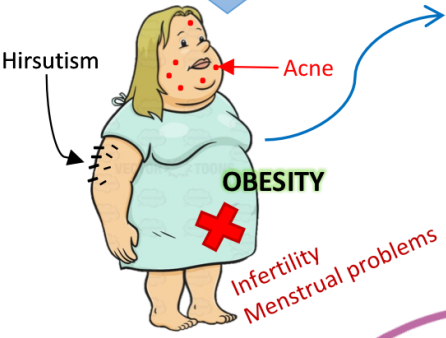
Red: Important.

Grey: Extra Notes

Doctors Notes

## Clinical Appearance

15 - 30 years



## Women at risk for

- Endometrial hyperplasia & endometrial cancer
- Insulin resistance/Type II diabetes
- High blood pressure - Depression/Anxiety
- Dyslipidemia - Cardiovascular disease
- Strokes - Weight gain
- Miscarriage - Acanthosis nigricans
- Autoimmune thyroiditis

**Polycystic Ovarian Disease (Stein-Leventhal Syndrome)**

It is the bilateral enlargement of ovaries by multiple small cysts

↑LH & ↓FSH

## Treatment

- Reduction of ovarian volume by wedge resection of the ovaries.
- Drugs that either induce ovulation or regulate the menstrual cycle.



## HISTOLOGY

**OVARIES:**

Outer portion of cortex is

- Thickened
- Fibrotic (w/ multiple cysts underneath)

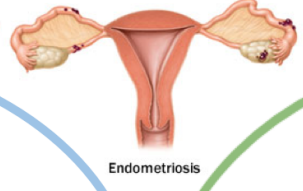
Corpora lutea are frequently absent due to anovulation

**ENDOMETRIUM:**

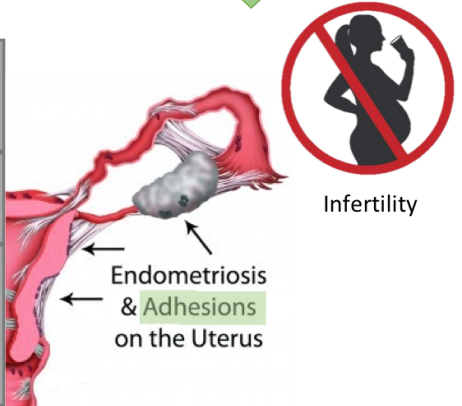
Chronic anovulation → hyper estrogenic state

Appearance ranges from: Mild hyperplasia to complex hyperplasia to atypia to endometrial adenocarcinoma

## Clinical Appearance



## Complications

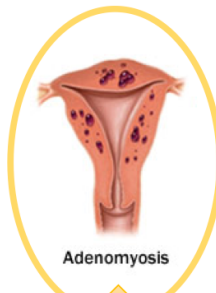


**Endometriosis**

It is the presence of ectopic endometrial glands and stroma outside the uterus.

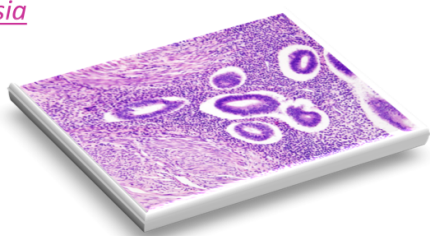
There is menstrual type bleeding at the site of the ectopic endometrium, resulting in blood filled areas (e.g. chocolate cysts). However, it is benign.

## Adenomyosis



- This is defined as the presence of endometrial glands and endometrial stroma in the myometrium of the uterus.
- It is associated with menorrhagia and severe dysmenorrhea.

- Ectopic endometrial glands and stroma are present
- Denatured blood from previous bleeding is present
- Macrophages containing hemosiderin (siderophages) are present.
- Hyperplasia



The lesions produce myometrial thickening with small yellow or brown cystic spaces containing fluid or blood.

# Polycystic Ovarian Disease (PCOD):

Bilateral enlargement of ovaries by multiple small cysts, chronic anovulation and clinical manifestations secondary to excessive production of estrogens and androgens (**mainly androgens**), **affecting both ovaries**.

- The initial abnormality resulting in the syndrome is **not known** but is believed to be related to **hypothalamus-pituitary dysfunction** leading to oversecretion of luteinizing hormone (LH).
- LH in turn stimulates the ovary to produce excess androgens. Secretion of follicle stimulating hormone (FSH) is inhibited resulting in suppression of ovulation with follicle cyst formation.
- High level of LH, testosterone & estrogen; and **low FSH**.
- Other names for this syndrome include **polycystic ovarian syndrome** and **Stein-Leventhal syndrome**.

## Clinical Appearance:

The usual clinical presentation is a young woman (between 15 and 30 years) with:

- Virilism due to excessive amounts or effects of androgenic (masculinizing) hormones.
- Secondary amenorrhea with anovulation
- Oligomenorrhea or irregular menses or **amenorrhea**.
- Infertility
- Hirsutism
- Obesity
- Acne

## Women with PCOS are at risk for the following:

- Acanthosis nigricans (patches of darkened skin under the arms, in the groin area, on the back of the neck)<sup>1</sup>.
- Endometrial hyperplasia and endometrial cancer.
- Cardiovascular disease.
- High blood pressure.
- Depression/Anxiety.
- Autoimmune thyroiditis.
- Insulin resistance (in T2DM).
- Dyslipidemia.
- Strokes.
- Weight gain.
- Miscarriage.

<b>Morphology</b>	<b>Ovaries</b>	<b>Gross</b>	Ovaries are 2 times the normal size with many subcortical and cortical cysts measuring 0.5 to 1.5 cm in diameter. The “cysts” in polycystic ovaries are not true cysts, but rather antral follicles which have arrested in development.
		<b>Microscopically</b>	<ul style="list-style-type: none"> <li>▪ The outer portion of the cortex is thickened and fibrotic (cortical stromal fibrosis) with multiple cysts underneath.</li> <li>▪ The follicular cysts usually have a prominent <b>theca interna</b> layer.</li> <li>▪ Corpora lutea are frequently absent due to the anovulation.</li> </ul>
	<b>Endometrium</b>	The unopposed estrogenic due to chronic anovulation leads to a hyper estrogenic state; hence, endometrium may show a variety of appearances ranging from mild hyperplasia to complex hyperplasia to atypia to endometrial adenocarcinoma.	

## Treatment:

Oral contraceptives and for the anovulatory cycle give drugs that induce ovulation if the patient wants to be pregnant.

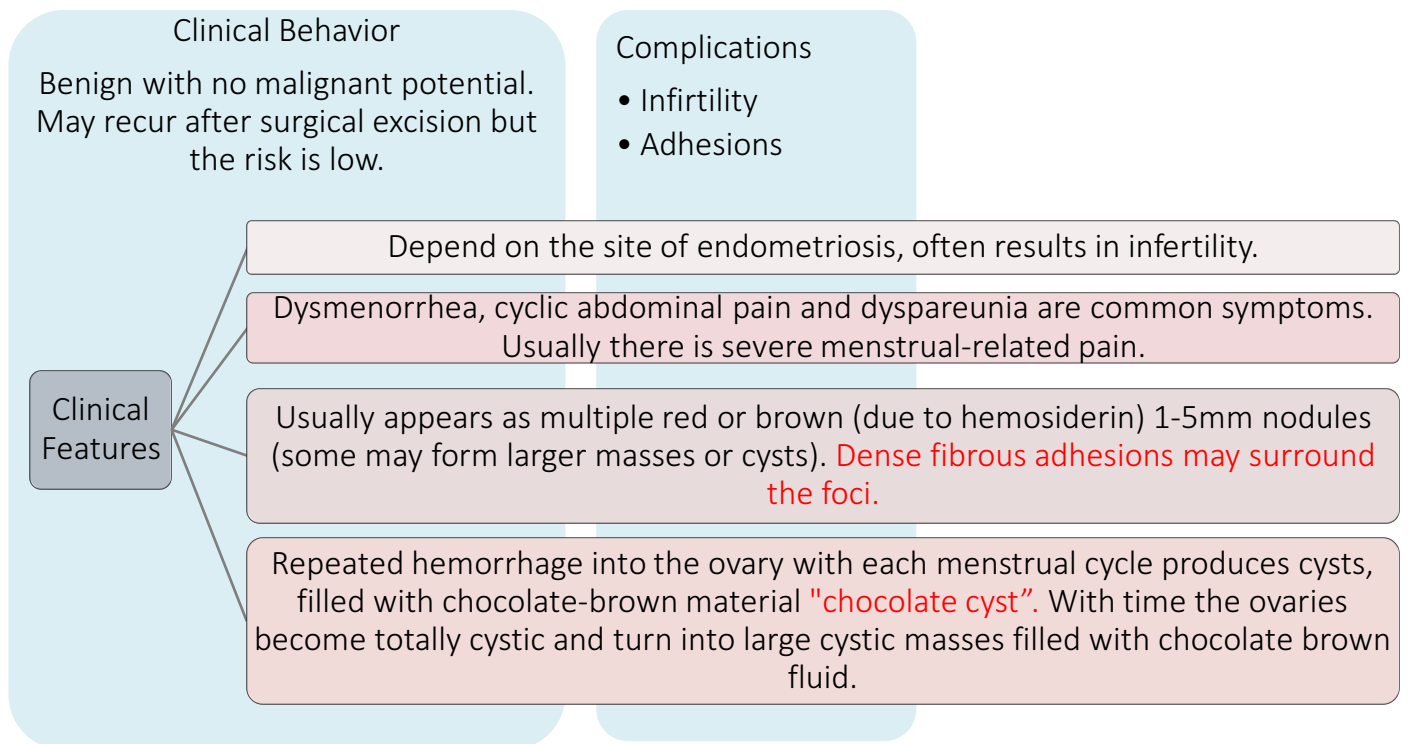
<sup>1</sup> Hyperinsulinemia leads to insulin spillover into other tissues, most commonly the skin. Insulin acts via insulin-like growth factor receptors to cause excess keratinocyte growth, producing velvety skin patches known as acanthosis nigricans.

# Endometriosis:

It is the presence of ectopic endometrial glands and stroma outside the uterus. **Non-neoplastic**. Normally: Endometrial glands and endometrial stroma are found in the endometrium of the uterus.

- It occurs in 10% of women in their reproductive years and in nearly half of women with infertility.
- Usually found on the peritoneal surfaces of the reproductive organs and adjacent pelvic organs.
- **The most frequent location is the ovary** (approx. 50%) followed by the pouch of Douglas & uterine ligaments.
- Occasionally involves cervix, vagina, perineum, bladder, large bowel and the umbilicus. Rare lesions are seen in as far as small bowel, kidneys, lungs, nose and brain.
- It has been reported in men. The sites involved were the bladder, scrotum and prostate.
- **Like** the uterine endometrium, it is **responsive** to the hormonal variations of the menstrual cycle, and bleeds during menstruation.
- Therefore, in endometriosis there is menstrual type bleeding at the site of the ectopic endometrium, resulting in blood filled areas (e.g. chocolate cysts).

## Clinical Features:



## Morphology:

- Ectopic endometrial glands and endometrial stroma are present.
- Denatured blood from previous bleeding is present.
- **Macrophages** containing **hemosiderin (siderophages)** are present.
- When endometriosis develops in a muscular organ, the smooth muscle around it is often hyperplastic.

**Theories behind pathogenesis:** 3 hypotheses explain the origin of these dispersed lesions.

- **The regurgitation theory** (currently favored), proposes that menstrual backflow through the fallopian tubes leads to implantation.
- **The metaplastic theory**, posits endometrial differentiation of coelomic epithelium (from which endometrium originates) as the source.
- These two theories cannot explain lesions in the lymph nodes, skeletal muscle, or lungs. Hence, the **vascular or lymphatic dissemination theory** has been invoked to explain extrapelvic or intranodal implants.

## Adenomyosis:

This is defined as the presence of endometrial glands and endometrial stroma in the myometrium of the uterus. **More common** in the posterior wall than the anterior wall (but it may affect both walls in the same uterus).

- The disease is primarily a disorder of parous women and is uncommon in the nullipara.
- The aberrant presence of endometrial tissue induces reactive hypertrophy of the myometrium, resulting in an enlarged, globular uterus, often with a thickened uterine wall.
- It is associated with menorrhagia and severe dysmenorrhea. In 1/3rd of the patients: there are no symptoms.
- When extensive the lesions produce myometrial thickening with small yellow or brown cystic spaces containing fluid or blood.
- Because the glands in adenomyosis are derived from the stratum basalis of the endometrium, **they do not undergo cyclic bleeding.**
- **Less severe than endometriosis.**

## Clinical behavior:

A benign condition with no known malignant potential that regresses after the menopause.



# Extra Summaries, Pictures and helpful explanations

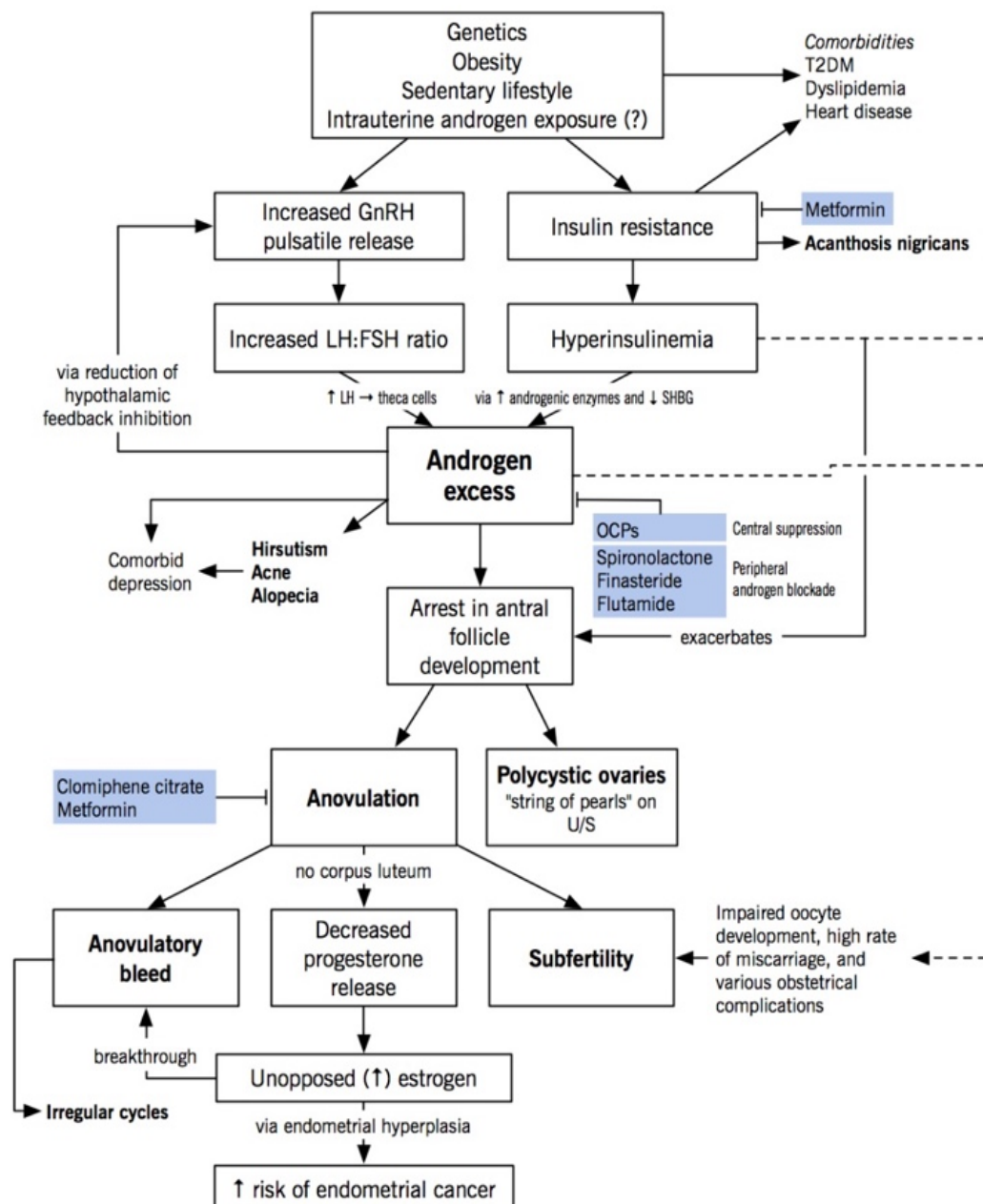
## Treatment of PCOS

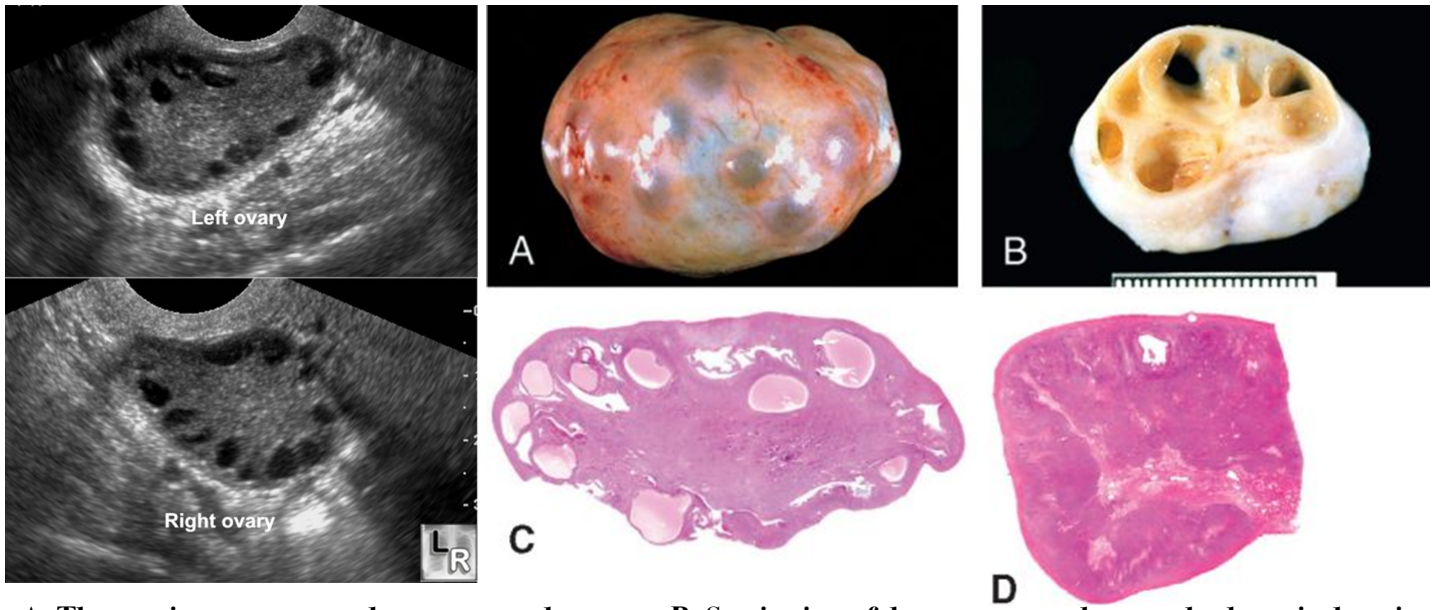
- Treatment with drugs that either induce ovulation (clomiphene or hCG) or regulate the menstrual cycle restores fertility.
- Reduction of ovarian volume by wedge resection of the ovaries is also successful in initiating ovulation and restoring fertility.
- The endometrial changes usually regress once ovulation is achieved.
- Weight loss of as little as 5-10% has been demonstrated to correct oligoanovulation and improve the ability of women with PCOS to conceive.

## Polycystic Ovarian Disease:

### Pathophysiology of PCOS

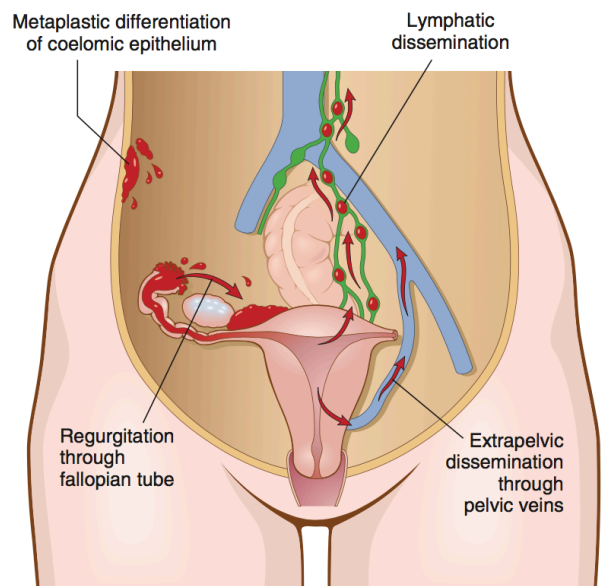
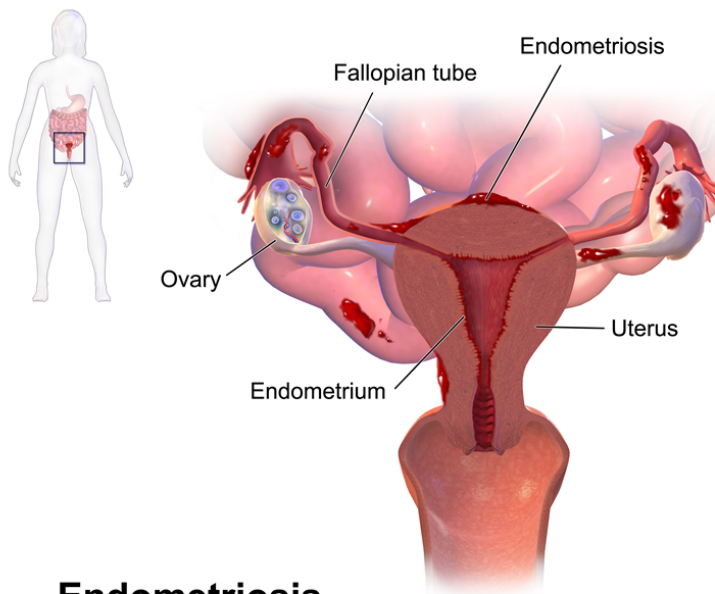
Alex Rotstein, Ragini Srinivasan, and Eric Wong





**A, The ovarian cortex reveals numerous clear cysts. B, Sectioning of the cortex reveals several subcortical cystic follicles. C, Cystic follicles seen in a low-power microphotograph.**

**Endometriosis:**



**Figure 18-9** Proposed origins of endometriosis.

**Endometriosis**

**Adenomyosis:**



Cross section through the wall of a hysterectomy specimen of a 30-year-old woman who reported chronic pelvic pain and abnormal uterine bleeding. The endometrial surface is at the top of the image, and the serosa is at the bottom

# Now Check Your Understanding!

## MCQs:

- 1. Are women with endometriosis in risk of cancer?**
  - A. Yes, slightly.
  - B. Yes, up to 80%.
  - C. Not at all.
- 2. Which of the following is not associated with PCOS?**
  - A. Obesity
  - B. Hirsutism
  - C. Adhesions
  - D. Infertility
- 3. Which of the following is the underlying pathophysiology explaining acanthosis nigricans in PCOS?**
  - A. Hyperinsulinemia
  - B. Hyperlipidemia
  - C. Hypertention
  - D. Elevated estrogens
- 4. Which of the following is correct about endometriosis?**
  - A. Most common site is the pouch of Douglas
  - B. Presence of hemosiderin pigment is diagnostic
  - C. Lesion seen in myometrium
  - D. Associated with high malignant potential
- 5. What is the most common site of endometriosis?**
  - A. Myometrium
  - B. Perimetrium
  - C. Fallopian tubes
  - D. Ovaries

## SAQ

A 34-year old woman came for a follow up after 6 months of her C-section, giving birth to a healthy girl, she asked the doctor about a nodule in her abdomen (in the subcutaneous tissue), which causes her discomfort whenever she is on her period. After removal of that nodule the pathologist reported the presence of a normal type of tissue in an abnormal area.

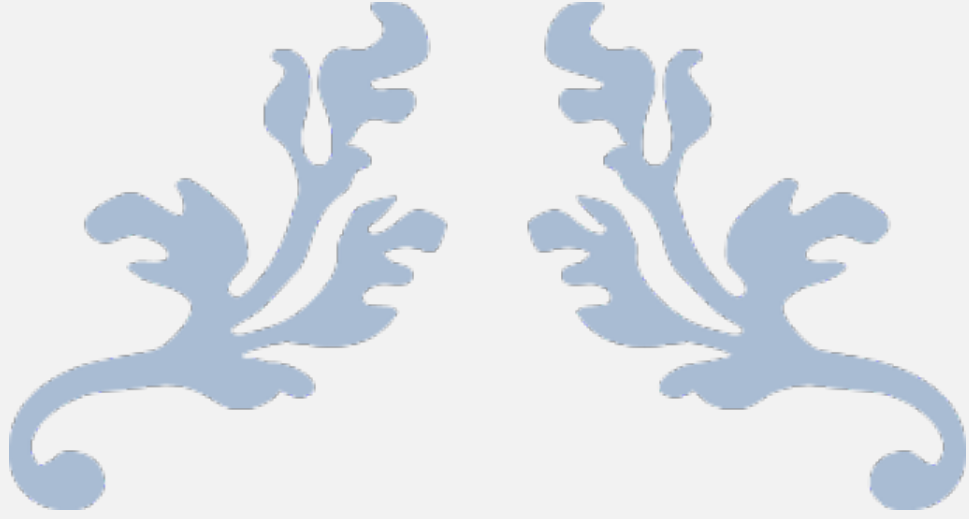
- 6. What is the type of tissue?**
- 7. How did she get it?**

### MCQs:

1: C    2:C    3:A    4:B    5:D  
6: Endometrial tissue  
7: She got it by the surgeon who mistakenly translocated some endometrial tissue to the abdomen.







Thanks for checking our work! Good Luck.

Done by:

نوف التويجري & عمر آل سليمان

ديما الفارس

فرح مندوزا

لينا الشهري

{ قال صلى الله عليه وسلم: من سلك طريقًا يلتمس فيه علمًا سهل الله  
له به طريقًا إلى الجنة }

